given time for the brain to readjust itself in some degree to the changes of pressure following the opening of the dura.

Hernia cerebri is a serious complication of operation for brain tumor. Where it results from decompression it has been supposed to be indicative of the degree of intracranial pressure and to show to what extent intracranial pressure has been relieved. This view is not entirely correct. Intense intracranial pressure possibly may be more liable to cause hernia than intracranial pressure that is more nearly normal, and yet much hernia may develop where there has been no decided increase of intracranial pressure. A large hernia occurred in one of my cases in which a thrombus of the inferior petrosal sinus of long duration had caused atrophy of the adjoining pons, the intracranial pressure could not have been greatly increased, nevertheless a large hernia developed. It seems probable that in such cases acute swelling of the brain in the sense of Reichardt may be responsible for the hernia.

A hernia may cause pressure against the edges of the opening in the skull, with occlusion of vessels and softening of the parts of the brain implicated in the hernia, causing in this way hemiplegia and other grave symptoms.

I am indebted to Dr. A. J. Smith for the photographs.

THE MECHANISM OF THE CIRCULATORY FAILURE IN DIPHTHERIA.

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In the course of acute infections it is well known that the patient may die with symptoms somewhat like those of surgical shock. The blood-pressure falls, the pulse becomes weak and small, the skin is pale or cyanotic about the nose and ears, sweating and vomiting ensue, and with shallow respiration and general collapse, the heart stops beating.

The discussion as to the mechanism of this disturbance is so well known that only the briefest *résumé* need be given here. It had long been thought from clinical observations that the affection might be one of the vasomotor apparatus rather than the heart itself, and Romberg, Pässler, Brühns, and Müller attempted to prove this in the case of diphtheria, pneumococcus, and pyocyaneus infections by experimental studies. In these studies they relied upon certain methods which aimed to demonstrate that the heart would regain its activity if the failure of the vasomotor apparatus were overcome in some way, and that those things which ordinarily caused vasomotor reactions were ineffectual. Thus they found that the mechanical expression of the blood from the splanchnic veins into the heart would restore for a time the aortic pressure, and with that the coronary blood-supply, and thus the nutrition and activity of the heart. The same could be produced by compressing the aorta. Barium chloride still caused the vessels to contract, but sensory stimuli had lost their effect. They, therefore, concluded that the circulatory failure was not due primarily to injury of the heart, but rather to the paralysis of vasomotor centres in the brain, which, causing a lowering of arterial resistance, quickly affected the heart through the diminished coronary supply to the heart wall. Romberg especially pointed out the fact that if the heart were at fault all these tests should fail.

Then Stejskal criticized their methods, showing that abdominal massage could increase arterial pressure even in a dead animal, and that its effects are very transient. He believed that the heart itself is directly injured, and fails on that account. Gottlieb supported this view to some extent, believing that the withdrawal of blood from the coronary circulation need not kill the heart so rapidly, since a heart may be kept for hours after the animal's death and then revived by perfusion. He therefore concluded that death probably was due to respiratory stoppage, with subsequent failure of the heart, due to its injury by the poison.

Rolly and Pässler later reviewed the subject, and seem to admit the force of Stejskal's objections as to the abdominal massage; and though they maintain the idea that the injury to the heart is through malnutrition, they state that it becomes very susceptible to other injuries. Other writers, whose papers are referred to below, lean to one or the other view or accept the idea that both vasomotor paralysis with its consequences and direct injury to the heart wall occur.

In the course of a study of the mechanical conditions present in aortic insufficiency, a plan was devised by which the influence of the vasomotors might be almost entirely eliminated and the work of the heart studied by itself.[1] This plan consisted in simply dividing the aorta near its root and connecting it with a long rubber tube, ending in a curved glass outlet, which could be elevated to any height upon a graduated upright pillar. The aortic pressure could in this way be set at any point according to the height to which the heart must drive the blood against the force of gravity. The blood which escaped fell into a cistern and returned through another long tube to the distal part of the aorta. Of course, by applying this arrangement to an animal in the collapsed condition which follows poisoning with the diphtheria toxin, the injurious effects of paralysis of the vasomotors would be removed at once, and if the theory of the Leipzig school be correct, the heart should return to its normal activity and the animal continue to live.

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[1] W. G. MacCallum, Johns Hopkins Hosp., Bull., 1911, xxii, 107.

The following protocols will illustrate the results of this experiment:

Dog 1.—Weight, 8.9 kg. April 25, 1911, 1 A.M. The dog was given 1 c.c. diphtheria toxin intravenously. At 11 A.M. the animal was found lying sick in the cage. Carotid pressure was taken at 11.30. Chest was opened and the circulation arranged as described, the outlet being set at 130 cm., which was the carotid pressure before the operation. The heart beat well for two hours, after which there appeared great edema of the lungs, and the heart dilated and stopped. All of the organs were found to be edematous, and showed numerous ecchymoses. The heart beat regularly throughout, and the output was well maintained.

Dog 6.—Weight, 6.6 kg. May 3, 1911, 12.45 A.M. The dog was given 0.75 c.c. diphtheria toxin intravenously. At 1 P.M. the carotid pressure was taken, the aorta cut, and external circulation arranged. This was finished at 1.20 P.M., and the heart beat well until 3.10 P.M., when there was extreme edema of the lungs and of other organs. In the heart, which was otherwise grossly normal, there were many hemorrhages. Here as in the first case the heart continued active for two hours.

Dog 7.—Weight, 10.3 kg. May 5, 1911, 12.30 A.M. The dog was given 2 c.c. diphtheria toxin intravenously. At 12 noon the dog was apathetic and drowsy. At 2 P.M. it vomited and appeared very weak. Artificial or external circulation arranged at 2.40 P.M. and the heart beat at a pressure of 110 cm. blood until 5.35 P.M. At times the heart began to collapse and beat with great excursions, driving out relatively little blood. One dose of digitalin and strychnine was given, which restored it to its normal beat. During the latter part of the three hours there were violent general convulsions.

Dog 13.—Weight, 6 kg. April 2, 1913. The dog was given 3 c.c. diphtheria toxin intravenously at 10.30 A.M. It was found very sick at 4 P.M., and at 4.45 P.M. the external circulation was arranged, after which the heart beat quite well until 7.20, when the supply of blood failed and the experiment was stopped. There was some irregularity in the action of the heart, but on the whole it beat strongly for two hours and thirty-five minutes.

In order to have a good control observation, two dogs of the same size were given the same dose at the same time. It was intended to show that with the aid of the maintenance of arterial pressure one could be kept alive long after the other had died.

Dog 14 A, weight 10,560, female, and Dog 14 B, weight 10,900, male. Each dog was given 4 c.c. diphtheria toxin intravenously at 8 A.M., April 3, 1913. Both dogs had vomited and were depressed and weak at 5 P.M. Dog A was found lying stretched out stiffly and not breathing. Heart not beating. Artificial respiration was begun. Carotid pressure was very low. It was attempted to establish the external circulation, but through an accident the dog died. By this time, 5.35 P.M., Dog B was almost dead, and lay inert. Reflexes were gone, the eyes rolled about, and there were convulsive twitchings. External circulation was established at 5.45 P.M. and tracings of the heart-beat were taken until 8.35 P.M., a period of two hours and thirty-five minutes when the heart stopped, apparently only because it finally became necessary to use blood which had been kept several days.

DOGS 15 A and B, weighing respectively 11 and 10.3 kg., were given 4 c.c. diphtheria toxin at 8 A.M., April 8, 1913. At 3.55 P.M. both dogs were almost dead, lying quite apathetic with complete loss of reflexes and occasional convulsions. Dog A, whose blood pressure as taken from the carotid was very low, about 60 cm. of blood, was arranged with the external circulation and the outflow tube set at 85 cm. The heart-beat improved at once and continued from 3.30 to 4.40 P.M. In the meanwhile Dog B died at 3.20 P.M. The character of the pulse of Dog A, as seen in the tracing, varied spontaneously being rapid and strong at times and producing an abundant outflow, while at other times there was a slower collapsing beat, which propelled relatively little blood to the outflow. After one hour and ten minutes it became distended during a convulsion, and could not be made to beat again. It seemed that in this case at least the heart itself had been injured by the poison.

For comparison normal dogs were subjected to the same operation as shown in the following protocols:

DOG 2.—Weight, 6.9 kg. Anesthetized with chloretone April 28, 1911. External circulation complete at 3.30 P.M.; pressure set at 130 cm. blood, which equals about 100 mm. mercury. At 4.45 P.M. there was much oozing from cut tissues, and the heart became distended. Pressure lowered to 53 cm. and heart beat again. Some edema of lungs and of other tissues. Given a dose of digitalin, after which heart beat well until 6.30 P.M., when the dog was killed.

DOG 5.—Weight, 9.9 kg. Anesthetized with ether May 2, 1911. The external circulation was arranged through one intercostal space at 3.20 P.M., and the outflow tube was set at 130 cm. of blood. The heart beat well until 6.20, when the dog was killed.

The actual output per minute of each of these hearts cannot be accurately determined from the curves produced by this method, because much of the blood circulates through the head and forelimbs, but since the records were all made in the same way, it will give some idea of the character of the heart's work after diphtheria poisoning to compare the output from the artificial aorta with that in the case of the normal dogs.

DOG 7 (Diphtheria).—Weight, 10.3 kg. Outlet was set at 110 cm.

Operation at	2.40	P.M.				
	3.30	"	100 c.c.	were delivered in	20	seconds.
	4.00	"	100 c.c.	"	28	"
	4.30	"	100 c.c.	"	32	"
	4.35	"	100 c.c.	"	30	"

DOG 1 (Diphtheria).—Weight, 8.9 kg. Outlet was set at 130 cm.

Operation at	11.30	P.M.				
	12.00	M.	100 c.c.	were delivered in	18	seconds.
	12.30	A.M.	100 c.c.	"	19	"
	1.00	"	100 c.c.	"	19	"
	1.30	"	100 c.c.	"	18	"

DOG 2 (Normal).—Weight, 6.9 kg. Outlet was set at 130 cm.

Operation at	3.30	P.M.				
	3.50	"	100 c.c.	were delivered in	21	seconds.
	4.30	"	100 c.c.	"	20½	"
	5.45	"	100 c.c.	"	34	"

DOG 5 (Normal).—Weight, 9.9 kg. Outlet at 130 cm.

Operation at	3.00	P.M.				
	3.45	"	100 c.c.	were delivered in	35	seconds.
	4.30	"	100 c.c.	"	29	"
	5.00	"	100 c.c.	"	30	"
	5.30	"	100 c.c.	"	29	"

From these it will be seen that the actual work of the diptheria hearts was at least as good as that of the normal hearts.

It is probable that if the conditions were absolutely perfect and the exposure, use of defibrinated blood, etc., avoidable, it would be possible to keep a normal heart driving the external circulation for a longer time than three hours. It is probable, too, that even under the present circumstances a normal heart treated in the way the hearts of the poisoned animals were treated would beat a little longer and a little more steadily than they. But the difference is so slight that, while it seems probable from such spontaneous irregularities as occurred in the case of Dog 15 A, that the heart itself was injured by a large dose of toxin, it was clear enough that it was still able to carry on the circulation for two or three hours against a high pressure, a thing which is vastly different from mere beating in a profusion apparatus.

It might be objected that the use of fresh blood would restore the heart by washing away the toxin, but in all these experiments the blood of the animal itself was returned to the circulation and was merely diluted. At any rate, Decroly and Ronnse showed that diphtheria toxin injected into the blood stream disappears completely after four to seven minutes, so that the injury is probably determined in some early part of the latent period. Rolly in his experiments found that washing out an isolated heart with fresh blood had no effect in postponing the death of the heart, and apparently this was true. But while Rolly was unable to revive a poisoned heart, it proved to be not impossible, as the following protocols show.

DOG 16.—May 13, 1911. Isolated heart from normal dog perfused with Ringer's solution beat for two and a half hours at a rate of about 103. The drops of diphtheria toxin injected into the circulating fluid caused an immediate increase in rate to 200 after which the heart continued to beat for two hours longer at a rate of about 150.

DOG 17.—May 24, 1911. Isolated heart from normal dog perfused and was beating for one hour at a rate of 98. At 12.25 P.M. 1 c.c. of diphtheria toxin was added to perfusion fluid. This was followed by a marked stimulation of force and rate which rose to 112. The heart continued to beat until 3.30 P.M., when after a period of dissociation of auricular and ventricular beats it stopped.

DOG 18.—May 25, 1911. Weight, 5.7 kg. The dog was given 1 c.c. toxin intravenously at 11.10 A.M. At 6 P.M. the carotid pressure was low. At 10.30 A.M. the dog was extremely ill, and died at 10.55 A.M. The heart was found to have stopped beating. It was removed from the body and perfused with Ringer's solution, upon which it began to beat at 11.10 A.M., and continued to beat well for one hour and ten minutes.

DOG 19.—May 25, 1911. Weight, 5.9 kg. The dog was given 1 c.c. diphtheria toxin at 11.30 A.M. At 5.45 P.M. it was killed with ether and the heart excised and perfused with Ringer's solution. From 6.45 to 10.55 P.M. the heart beat strongly and regularly at a rate of about 90 to 110.

DOG 20.—May 25, 1911. Weight, 6.8 kg. Given 1 c.c. diphtheria toxin at 11.45 P.M. At 1 P.M. the next day the dog was nearly dead. It was killed at 1.35 P.M. and the heart perfused. The rate was somewhat irregular, varying from 44 up to 110, but for the greater part of the next two hours it beat strongly at about 62, stopping at 4.50 P.M.

DOG 21.—May 28, 1911. Weight, 7.8 kg. Given 2 c.c. of diphtheria toxin intravenously at 9.45 P.M. At 11 A.M. the next morning the dog was found dead, although alive and apparently fairly well a few minutes before. The heart was excised, but could not be started in perfusion apparatus until 11.50. At first there was fibrillation, but this was stopped by injection of potassium chloride, after which it beat somewhat irregularly until 2.15 P.M., a period of two hours and twenty-five minutes.

DOG 22.—May 30, 1911. Weight, 8.7 kg. Given 2 c.c. diphtheria toxin at 11 P.M. The next day at noon the dog died; the splanchnic vessels were much dilated. The heart was perfused at 12.15 P.M. and beat fairly well for three hours and forty minutes, becoming edematous at last. For most of the time the rate was 96 to 100, but several times a spontaneous heart-block occurred, with a 1 to 2 rhythm, which each time suddenly changed back to the 1 to 1 rhythm.

DOG 23.—May 30, 1911. Weight, 8.2 kg. Given 1.5 c.c. diphtheria toxin at 11 P.M. The next day at 3.15 P.M. the dog was evidently dying. It was killed with ether and the heart excised and perfused. Perfusion began at 4 P.M., and the heart beat with varying rate until 7.20, a period of three hours and twenty minutes.

DOG 24.—June 1, 1911. Weight, 7 kg. Given 2 c.c. diphtheria toxin at midnight. At 11 A.M. the next day the dog was *in extremis*. The carotid pressure was very low. Etherized, and the heart was excised and perfused. It beat slowly from 11.20 to 2.25 P.M., about three hours, at a rate of about 52.

DOG 25.—June 2, 1911. Weight, 7.2 kg. Given 2 c.c. diphtheria toxin at midnight. At 1.15 P.M. the next day dog was very sick. Alcohol by stomach-tube had no effect upon the blood pressure, which sank until the dog's death at 2 P.M. At 2.10 P.M. the heart was perfused and beat normally at a rate of about 94 for three hours and thirty minutes, stopping at 5.40 P.M.

DOG 26.—June 3, 1911. Weight, 8.9 kg. Given 2 c.c. diphtheria toxin at 11.15 P.M. The next morning, at 9.30 the dog was found dead but not cold. Rigor was beginning. At 9.45 A.M. the excised heart was perfused and beat until 10.40 A.M. at the rate of about 100, rather feebly and irregularly.

In all these hearts the beat was rather feeble as compared with that of the perfused normal heart, and fibrillation seemed likely to occur. The note reads: "There is no comparison between the perfused normal heart and the diphtheria hearts, all of which are feeble and apt to go into fibrillation." Nevertheless, although one may receive the impression that the hearts from the poisoned animals are rather weak and apt to be irregular, it is clear that they continue to beat for several hours after they have shown every sign of failure in the body of the dying animal, if only the pressure of nutritive fluid be maintained in the coronary arteries. Indeed, the animal may be allowed to die, and an hour after its death the heart can be revived and will beat for a long time. All of this seems to show fairly well that the death which occurs in the height of an attack of diphtheria is not exclusively the result of direct injury to the heart, although that may play some part in the process.

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BLEEDING IN TYPHOID FEVER.

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It is generally recognized that the occurrence of hemorrhage in the course of typhoid fever is a serious matter, especially when it appears late in the disease. The degree of seriousness of this complication, however, has been differently estimated by writers, and one finds Trousseau and Graves constantly quoted as declaring that it was not an unfavorable event and sometimes even of advantage, while Murchison, Dieulafoy,[1] and others state that it is a bad omen and not even of transient benefit. Thus, on the one hand, Leibermeister[2] writes: "If at the end of the third or fourth week a large intestinal hemorrhage appears, it may occur that the marked fall of temperature with it will have a favorable influence upon the enteric phenomena present, recovery steadily advancing from that time on. These are the cases that have led competent observers (Graves, Trousseau) to maintain that intestinal hemorrhages are by no means unfavorable in enteric fever, but are rather of favorable prognostic import." On the other hand, Murchison wrote: "Although I have seen patients recover after a profuse hemorrhage, I have never seen the slightest benefit from it."[3]

It is admitted by every writer that the temperature often tends to fall after a hemorrhage, but most state that along with this lessening in the temperature there is a rise in the rate of the pulse. Thus, for example, Curschmann[4] says: "In those cases in which the patient does not die during the first copious hemorrhage the clinical picture becomes alarmingly altered. The skin acquires a waxy

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[1] Text-book of Medicine (translation), ii, 1026.

[2] Modern Clinical Methods in Infectious Diseases, p. 30; The Physiology of Blood-letting, British Med. Jour., 1910, i, 104.

[3] Sir Thomas Watson, Principles and Practice of Medicine, ii, 881.

[4] Typhoid and Typhus Fevers, Nothnagel's Encyclopedia of Practical Medicine, p. 223.